



I. Overview (30 m)

- a. Brief history, aerosol exposures
- b. Equipment/animals
- c. Class III cabinets
- d. Procedural video

II. Aerosol generation (15 m)

- a. Overview of generation technologies
- b. Collision nebulizer
- c. Viability

III. Sampling & characterization (15 m)

- a. Methods of sampling (impinger, filter, etc.)
- b. Particle sizing
- c. Deposition and retention

IV. Dose (15 m)

- a. Definition of dose
- b. Calculation
- c. Importance of the 'spray factor'

BREAK

V. Emerging Technology (30 m)

- a. **Genesis of the automated technology**
- b. **Application**

VI. Examples: aerosol exp. of animals (30 m)

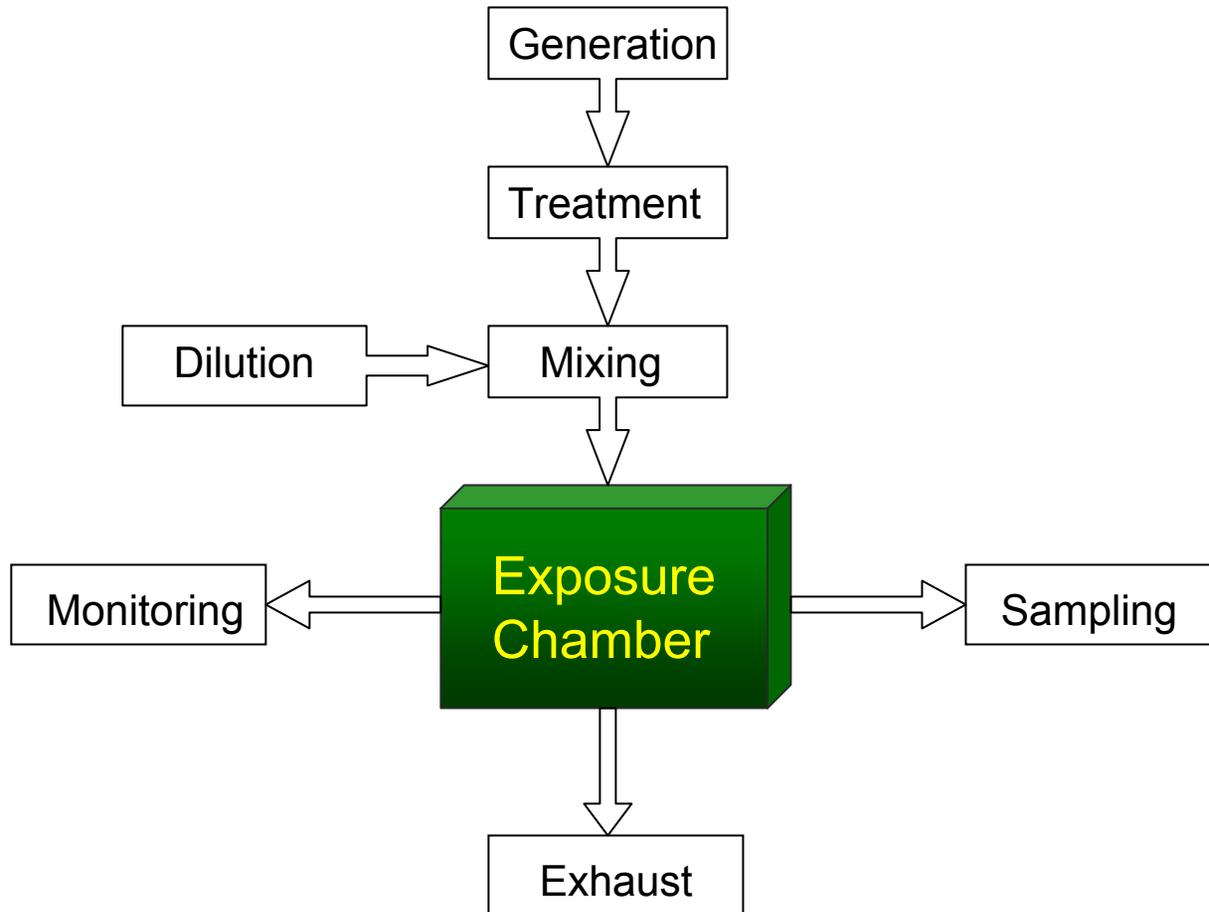


Development of an Automated Bioaerosol Exposure System

- Motivation
 - Manual control and hybrids of automation
 - Limited data acquisition in existing systems
 - Aerosol work is technically demanding
 - No standardization in aerosol work
- Objectives
 - Computer control of aerosol system
 - Improved control and data acquisition
 - Ease of use - “plug and play”
 - Standardized data recording and archiving
 - Integrate all aerosol functions into one platform
 - Improve dose *control* and dose *calculation*

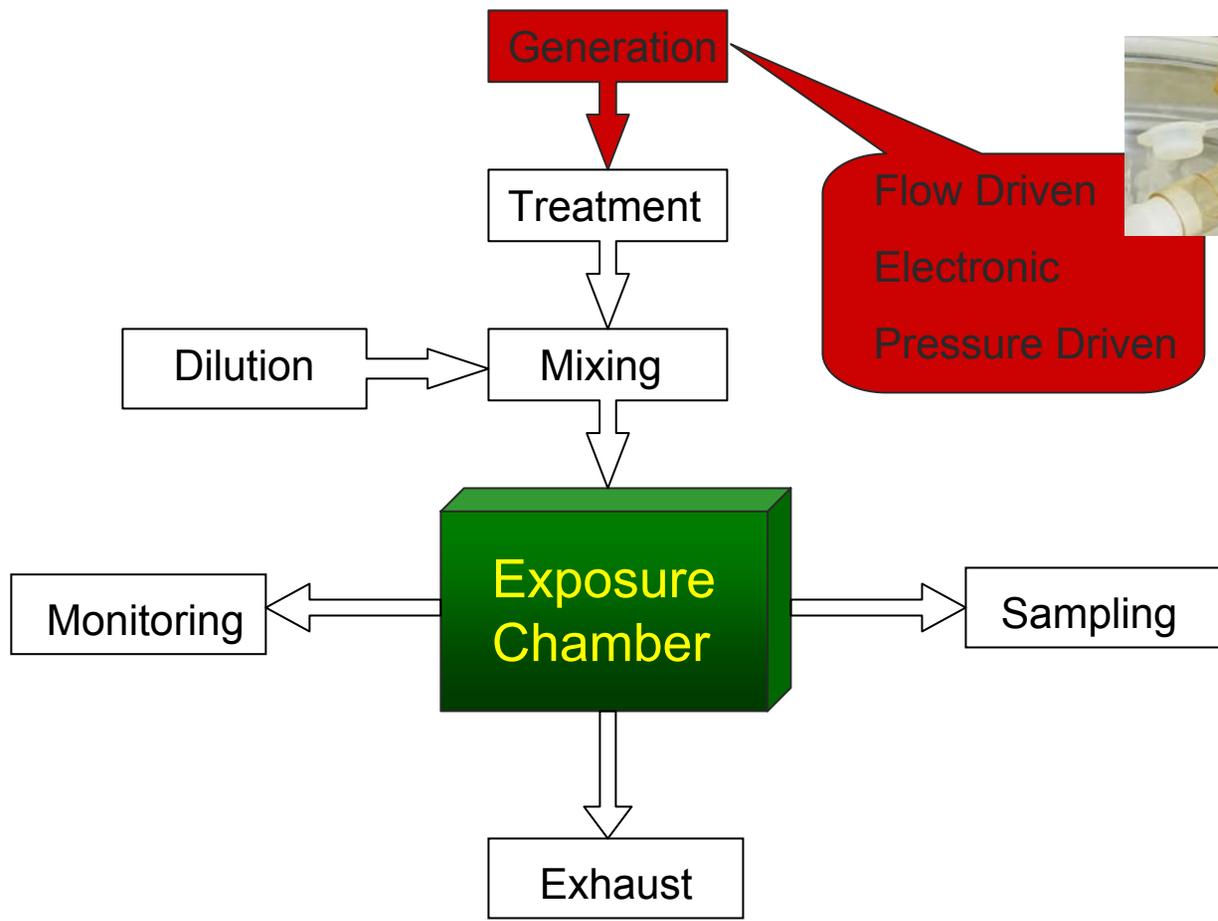


Dynamic System Components



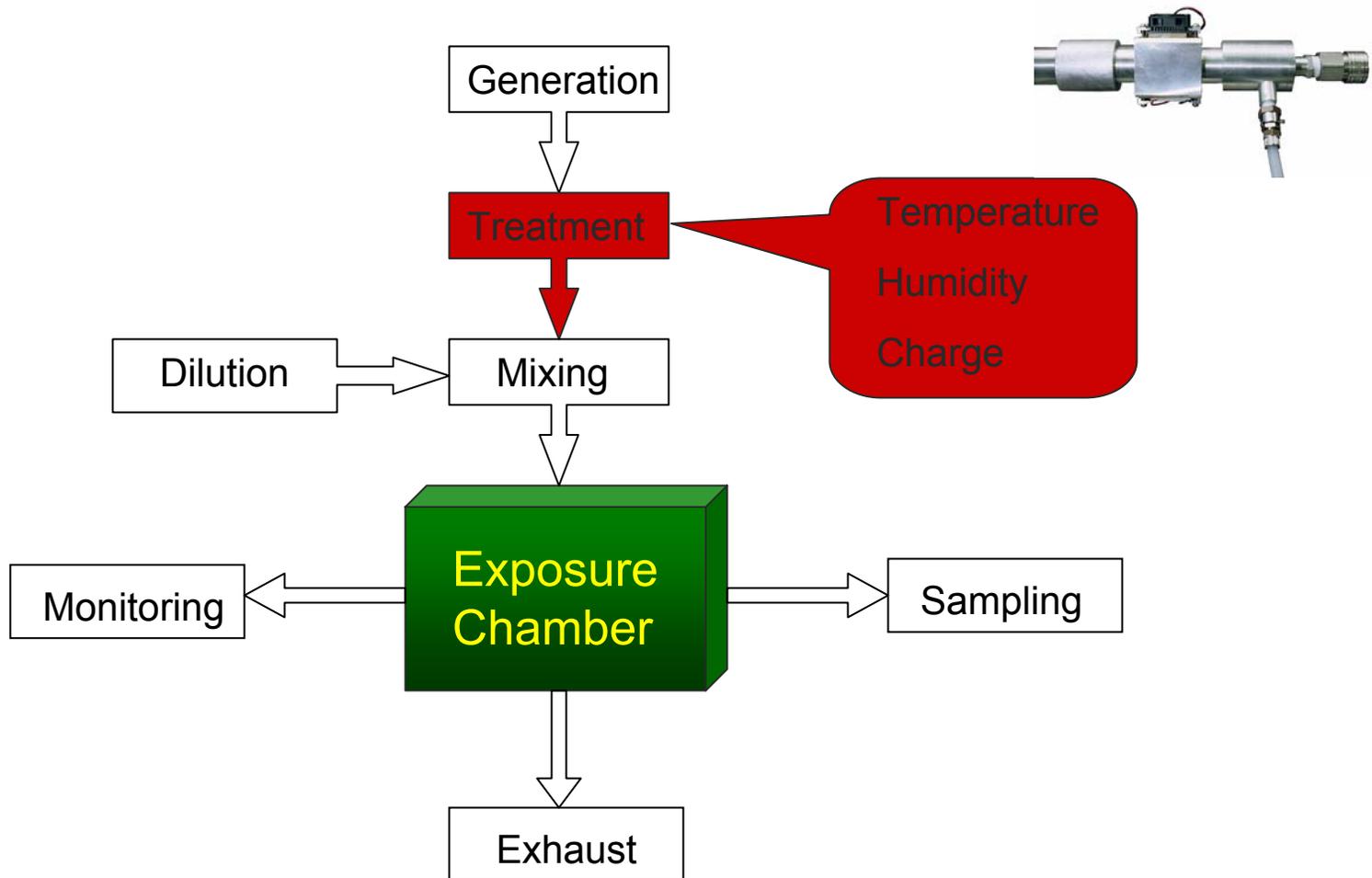


Aerosol Generation



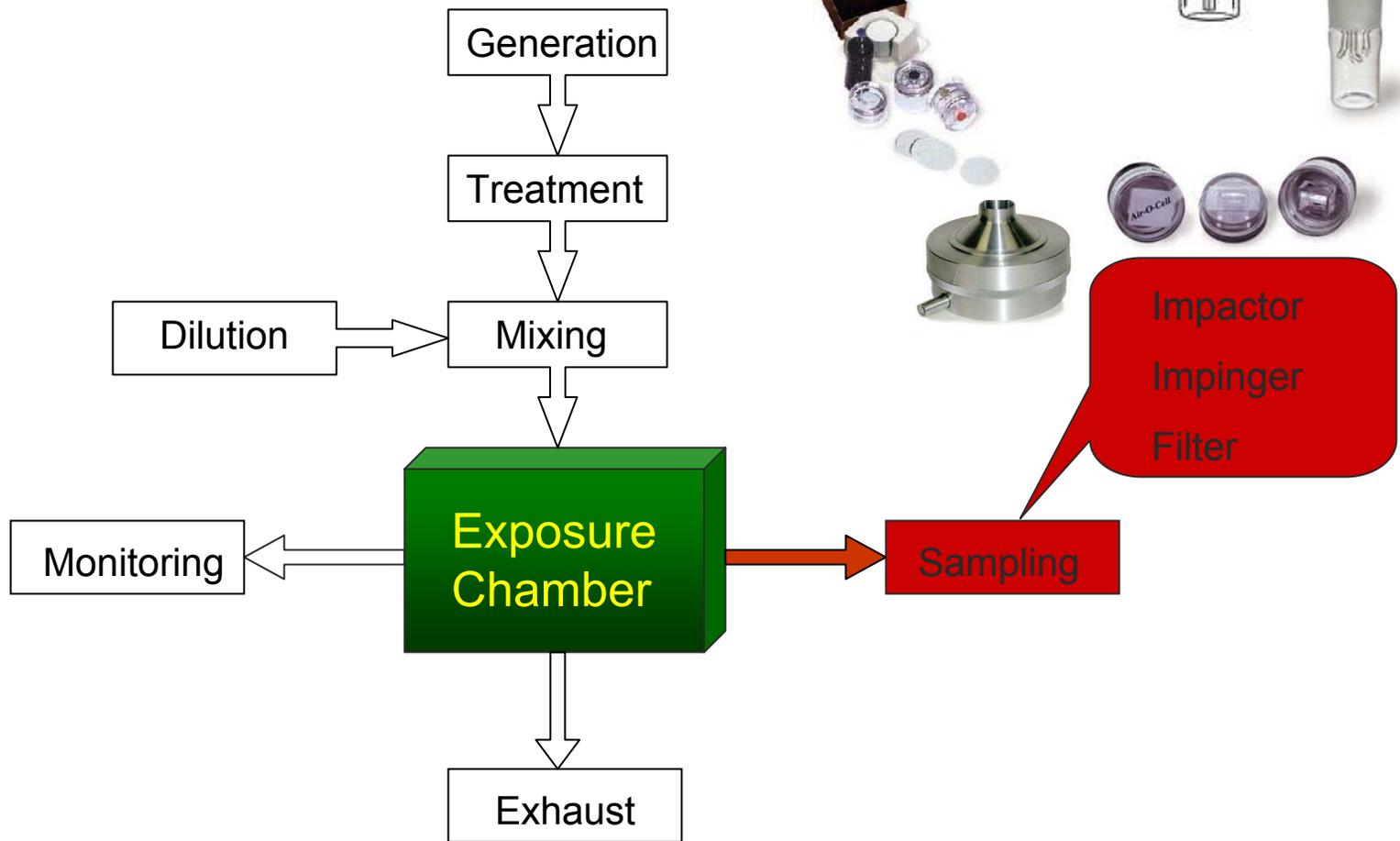


Aerosol Treatment



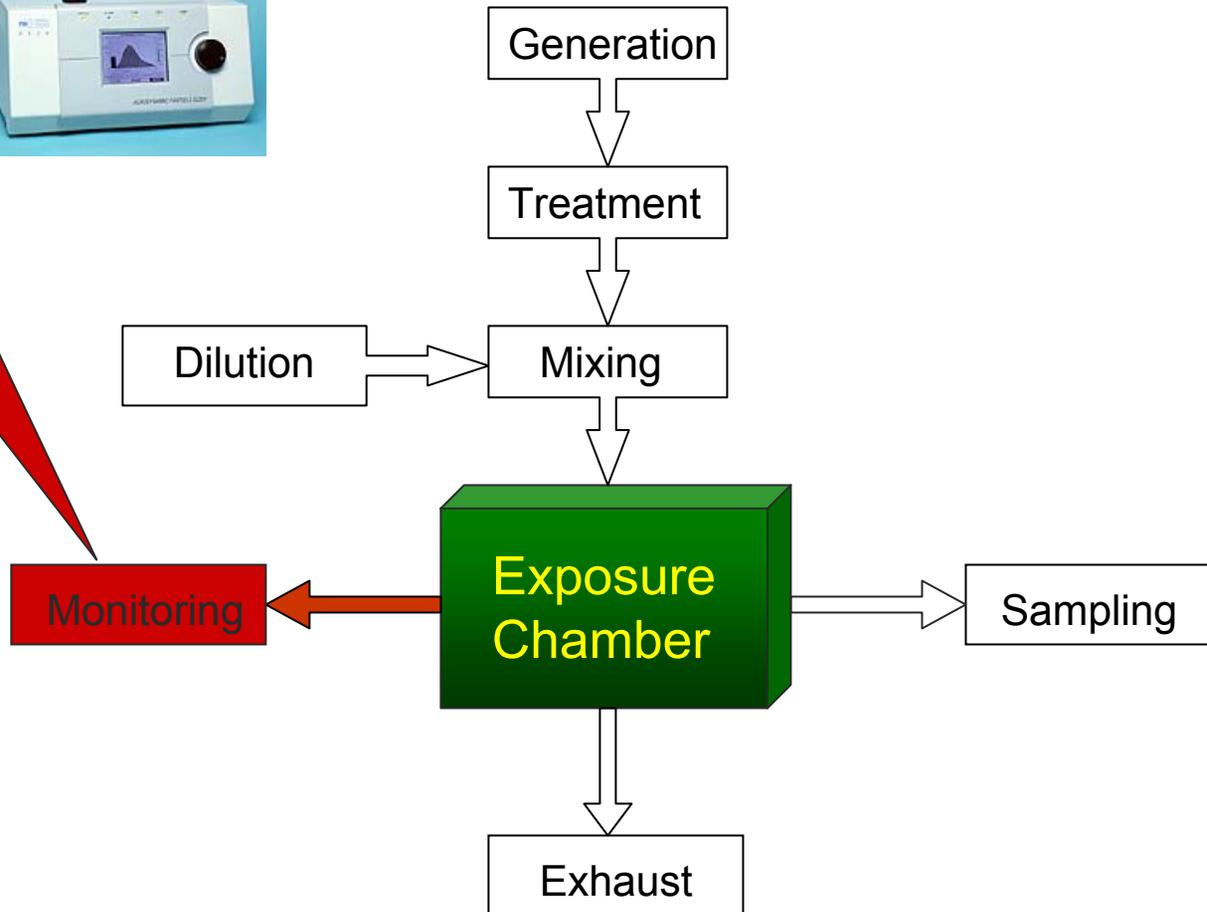


Aerosol Sampling





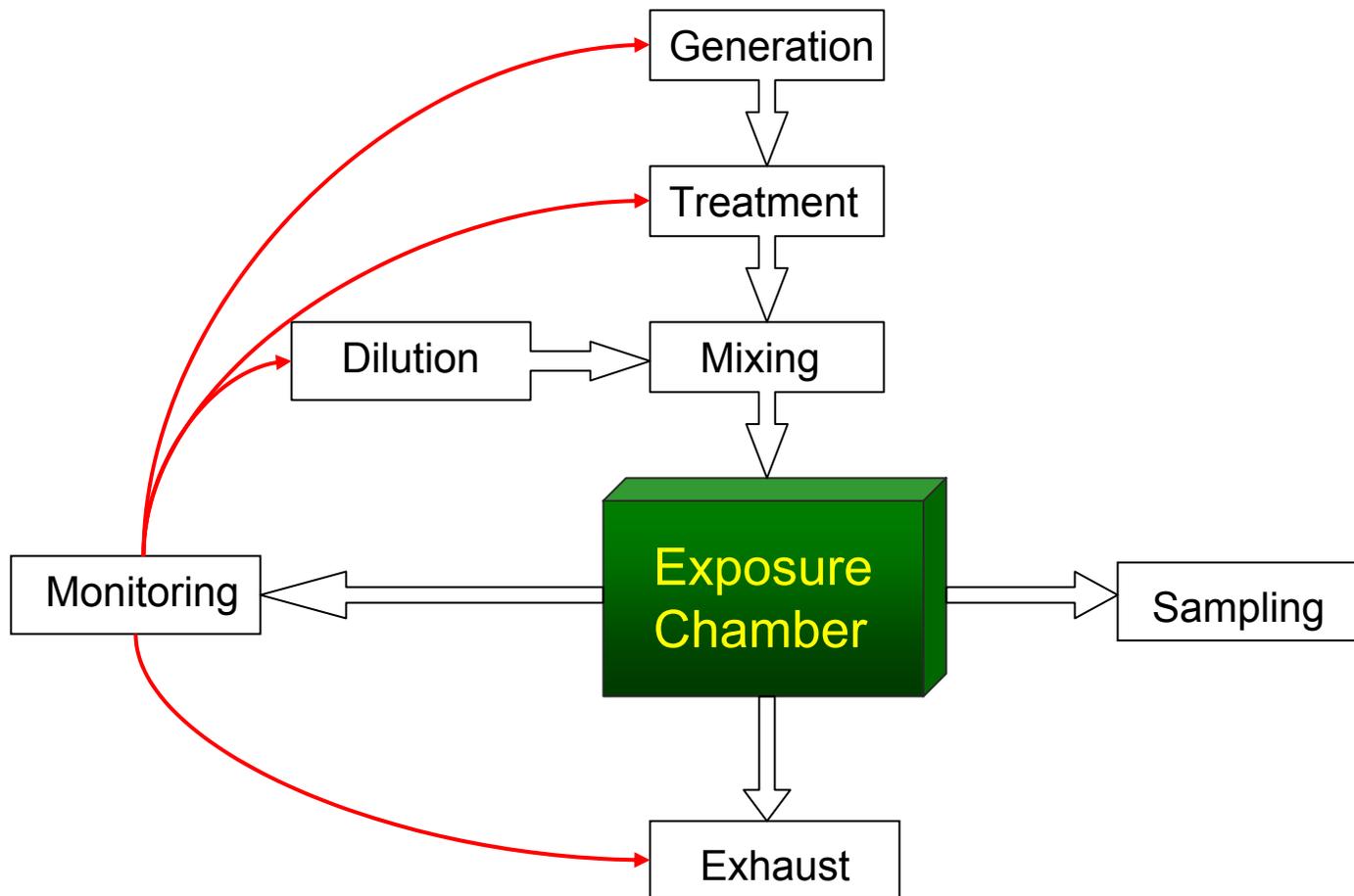
Aerosol Monitoring



Particle Size
Concentration
Environmental
Respiration
Pressure



Feedback

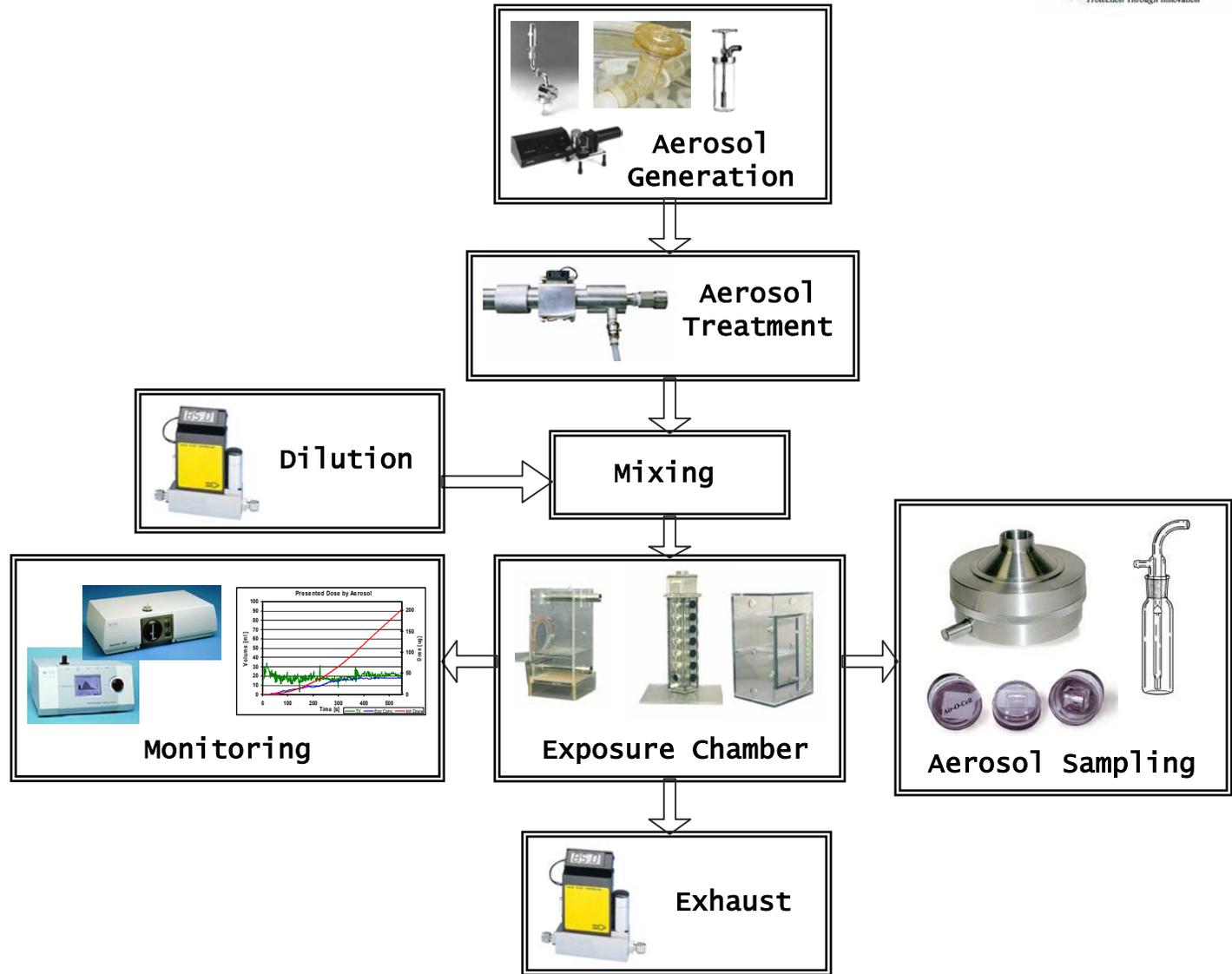




Aerosol Management Platform Concept and Operation



Aerosol Management Platform



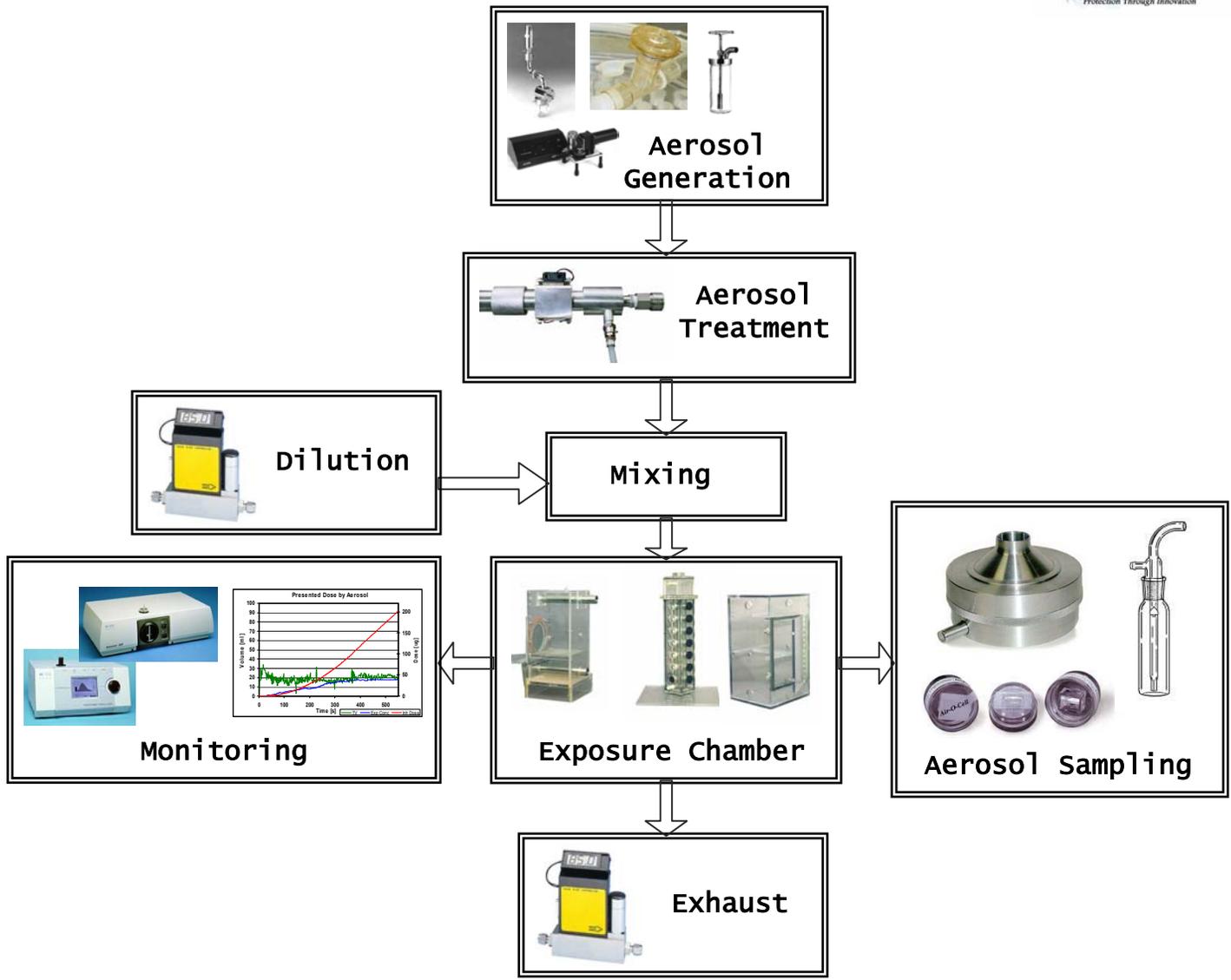


Aerosol Management Platform Concept and Operation



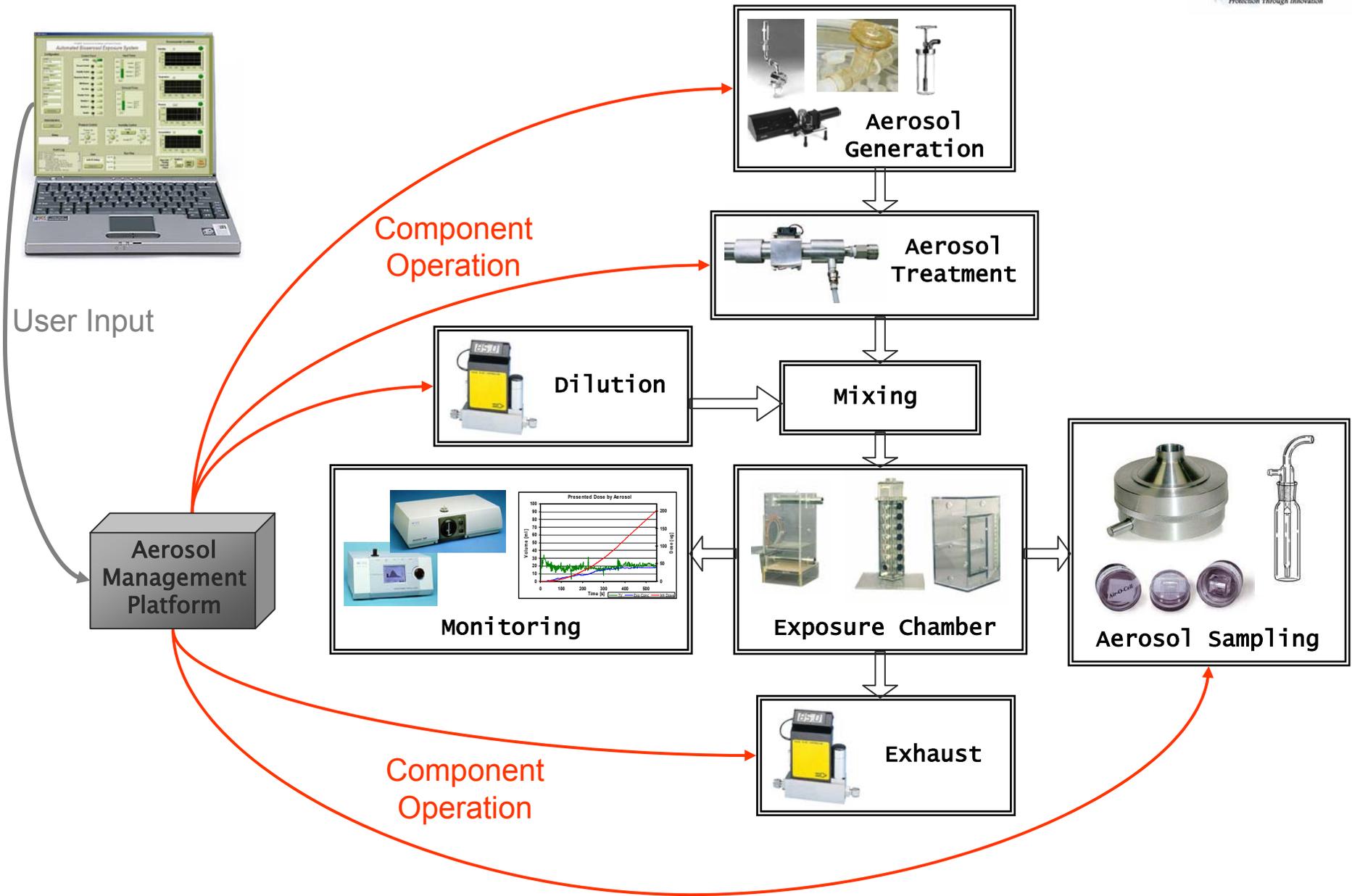
User Input

Aerosol Management Platform



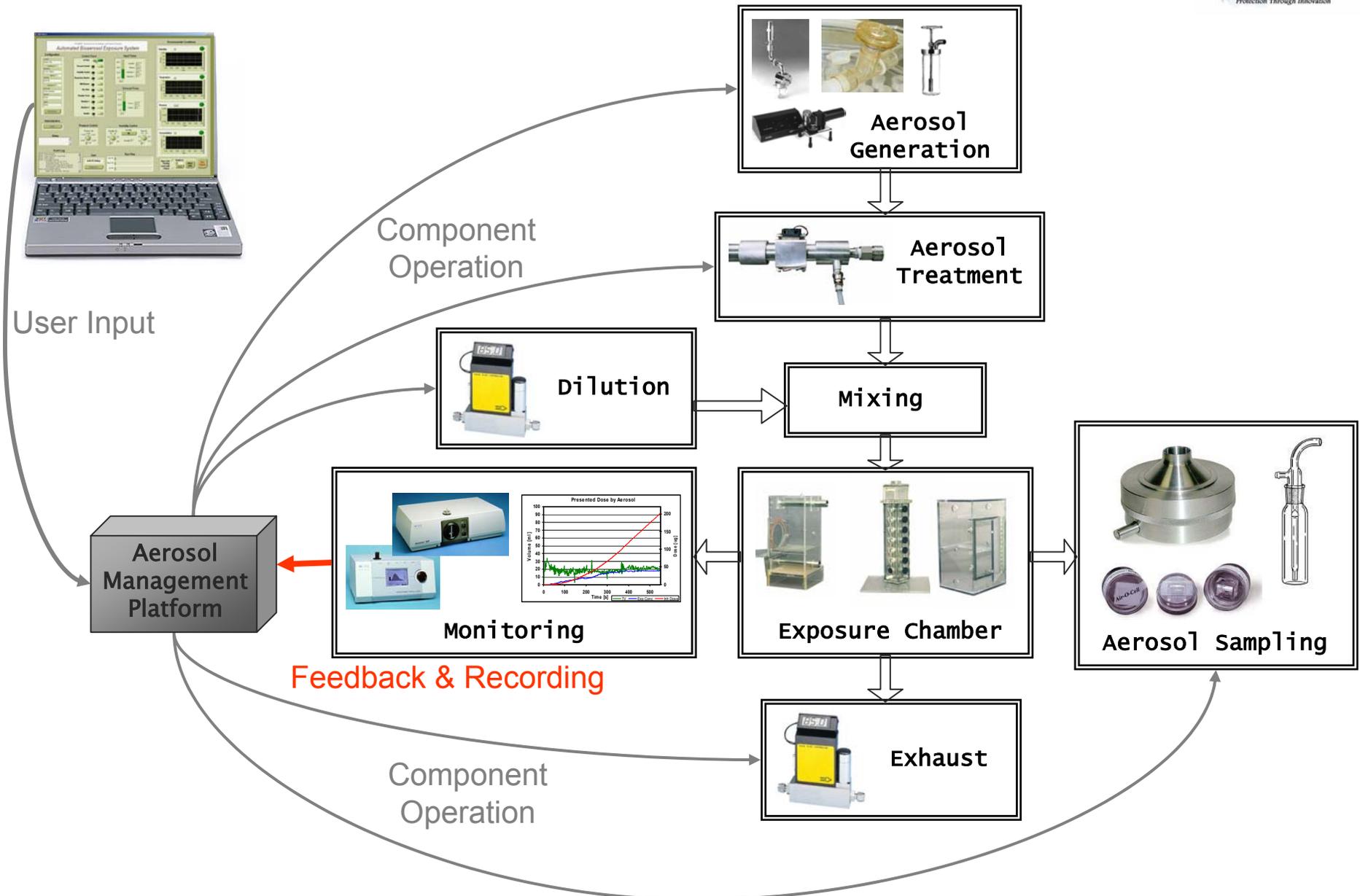


Aerosol Management Platform Concept and Operation



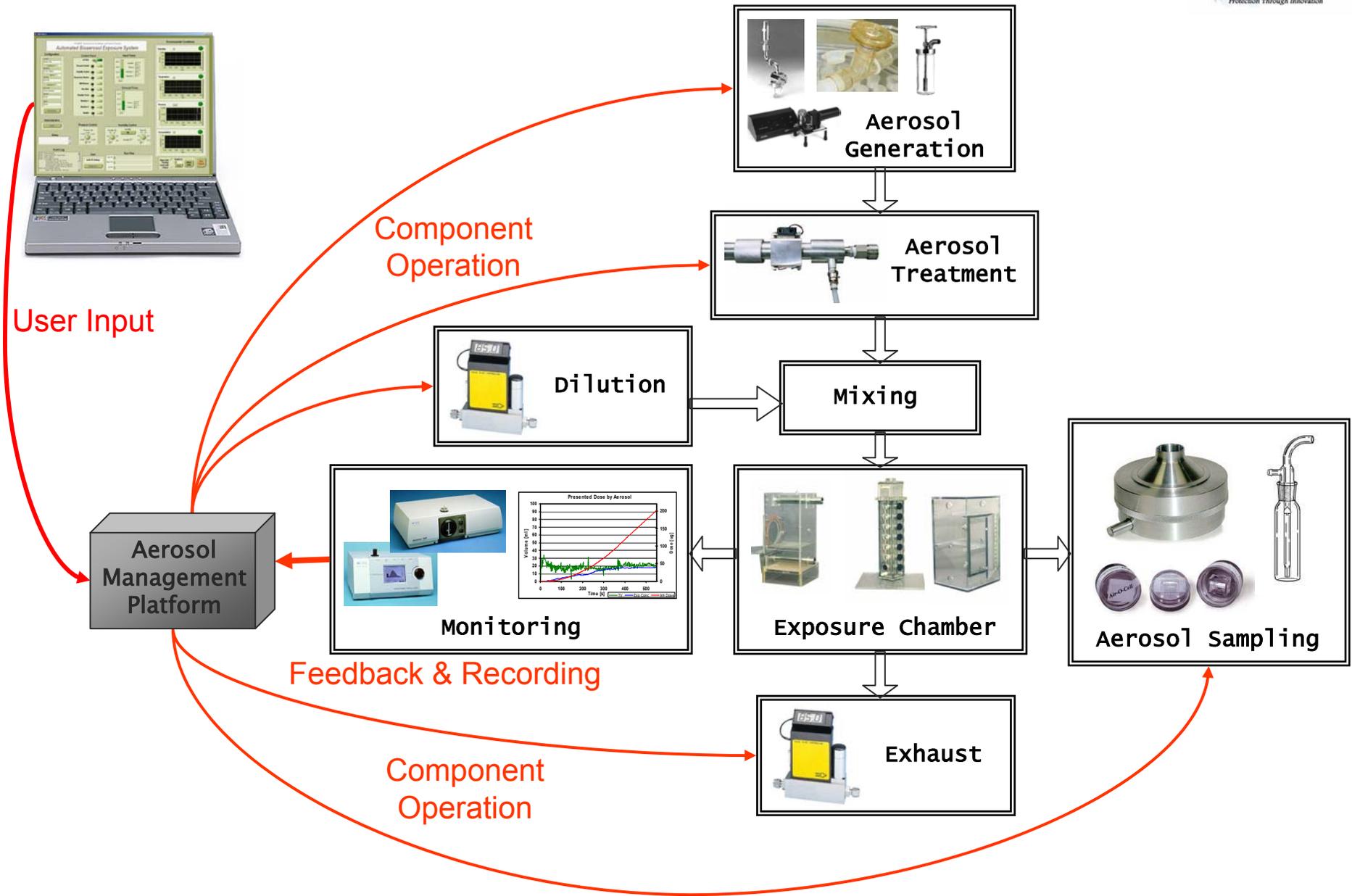


Aerosol Management Platform Concept and Operation





Aerosol Management Platform Concept and Operation

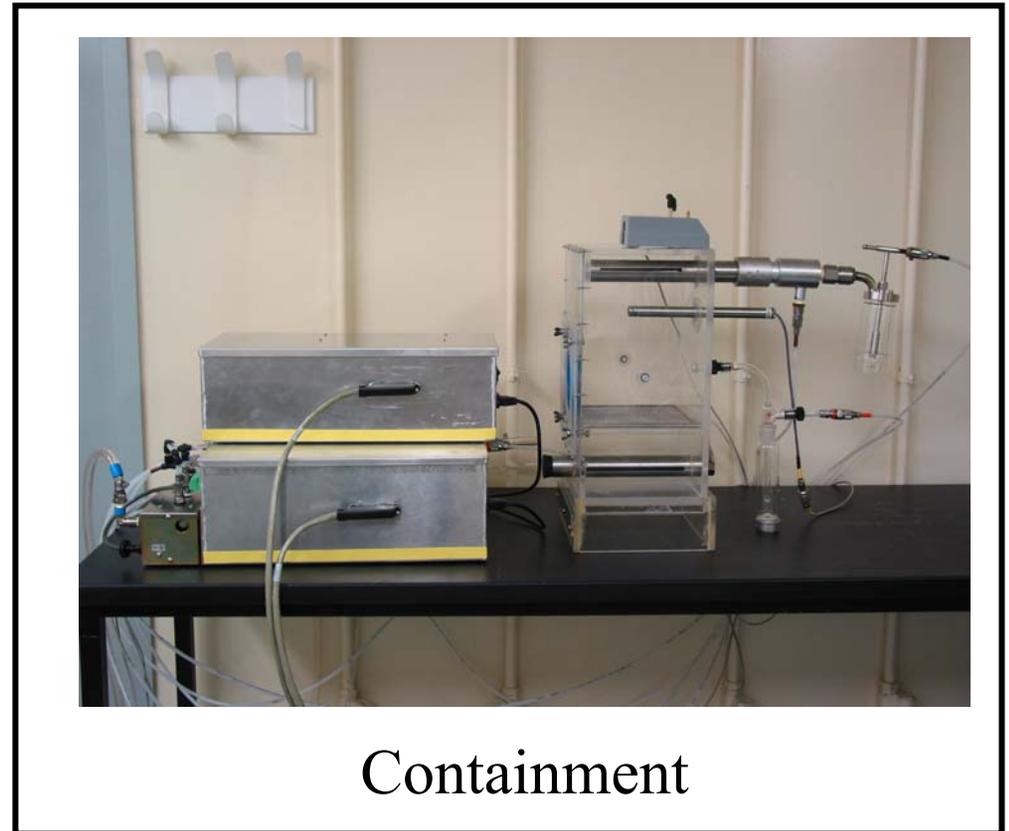




Overview



Workstation



Containment



System Hardware

- “Plug and Play” connections
- Electronic routing
- Power supplies
 - 12 Volt DC
 - Multi-tap AC transformer
- Mass flow controllers
- Relays
 - Electronic activation
 - Humidifier
- Multiple nebulizers or sampling devices





System Software

- Custom programmed using LabVIEW
- Single user accountability (electronic signature)
- Modular for environmental controls
- User configurable for hardware and exposure control
- Programmatic controls to prevent errors





Automated Bioaerosol Exposure System

Configuration

System
 Head Only
 System Q 16.0 lpm
 Nebulizer
 3 Jet Collision
 Neb Q 7.5 lpm
 Sampler
 AGI-30
 Sampler Q 6.0 lpm
 Exposure
 Dose Based
 Species
 NHP
 Agent
 Anthrax

Reconfigure

Administrative

Enter

Event Log

```
00:02:09 Display 55-55 Run 1 Started
Run: 1
AGI ID: 24
Animal: xx
Weight [g]: 5800
Sampler Vol [ml]: 10
Neb Conc: 3.000000E+8
Spray Factor: 7.000000E-7
Dose: 3.000000E+8
Save Period: 00:05
00:01:27 Run Parameters Entered
00:01:11 Humidity Setpoint Changed to: 60 %
00:01:07 Humidity Setpoint Changed to: 55 %
```

Control Panel

Air Flow

Pressure Control

Humidity Control

Nebulizer 1

Sampler

Run Start

Nebulizer 2

Respiratory Monitor

DBE Balance

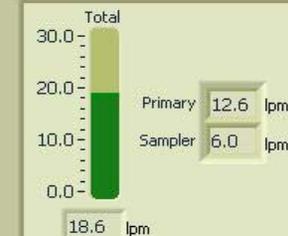
Pressure Control



Input Flows



Exhaust Flows



Humidity Control



Run Files

Data File C:\Program Files\National Instruments\Hartings\Display\55-55\Run 1\Display 55-55 Run 1 Data

Report File C:\Program Files\National Instruments\Hartings\Display\55-55\Run 1\Display 55-55 Run 1 Report.html

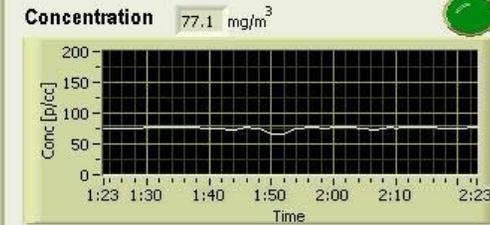
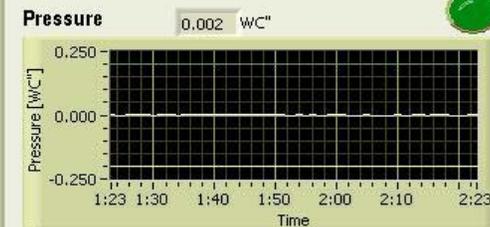
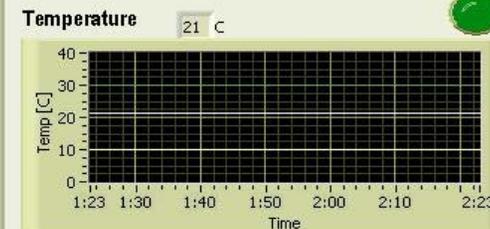
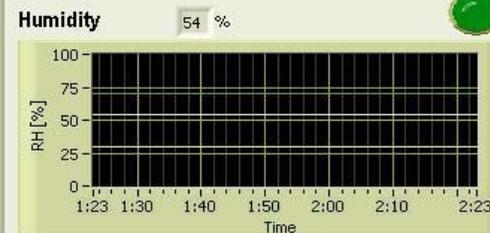
Log File C:\Program Files\National Instruments\Hartings\Display\55-55\Run 1\Display 55-55 Run 1 Log

User

Justin M. Hartings

E-Signature

Environmental Conditions



Upper Limit Reading

Lower Limit Failures

Sample (s) 1

Reset

Adjust Limits

Stop Program



System Event Log

- Time stamped event recording
 - Computer initiated
 - User initiated
- Single user accountability
- Quality management tool
- SOP compliance verification
- Troubleshooting
- FDA electronic filing

00:13:50	Concentration = 0 ug/L out of limits	
	Humidity Limits: 30 % to 70 %	
	Temperature Limits: 10 C to 30 C	
	Pressure Limits: -0.200 WC" to 0.200 WC"	
	Concentration Limits: 200 ug/L to 300 ug/L	
00:13:48	Environmental limits set	
00:11:54	Sampler On	
00:11:39	Pressure Normal	
00:11:38	Press = -0.230 WC" out of limits	
00:11:37	Nebulizer 1 On	
00:11:33	Nebulizer 1 Off	
00:11:16	Pressure Normal	
00:11:15	Press = -0.239 WC" out of limits	
00:11:13	Nebulizer 1 On	
00:11:04	Nebulizer 1 Off	
00:10:56	Pressure Normal	
00:10:54	Press = -0.230 WC" out of limits	
00:10:53	Nebulizer 1 On	
00:10:38	Nebulizer 1 Off	
00:10:22	Humidity Normal	
00:10:10	Pressure Normal	
00:10:08	Press = -0.241 WC" out of limits	
00:10:07	Nebulizer 1 On	
00:08:05	RH = 30 % out of limits	
00:04:14	Humidity Normal	
00:03:05	Airflow Started	
	Protocol Number: F03-11	
	Principal Investigator: Pitt	
	AED Number: 2003-	
	System Location: 119	
	Hoodline ID: 4	
	Generator Number: G	
00:02:22	Administrative Information Entered	
	System Type: Head Only - 16.0 lpm	
	Nebulizer Type: 3 Jet Collison - 7.5 lpm	
	Sampler Type: AGI-30 - 6.0 lpm	
	Exposure: Time Calculated	
	Animal Species: NHP	
	Agent: Plague	
00:00:50	System Configuration Entered	
00:00:06	Yellow System Selected	
	Network Drive N:\ Found	
00:00:00	E-Signature: Justin M. Hartings	
	User Login	
	Wednesday, October 29, 2003	
	08:38:06 AM Eastern Standard Time	



Data File

- Stand alone record of exposure
- Administrative data
- Flow and environmental data
- Part 11 compliant file system
- Automatic file structure development
 - Investigators
 - Animal use protocols
 - Exposure schedule



Exposure Data File



Justin M. Hartings														
Data File Started														
Wednesday, October 29, 2003														
11:41:25 AM Eastern Standard Time														
System:	Head Only	Protocol:		Run Number:	6	Neb Conc:	4.00E+06	cfu/ml						
System Flow [lpm]:	16	Principal Investigator:		AGI Number:	AA65	Spray Factor:	1.20E-06							
Nebulizer:	3 Jet Collison	AED Number:	2003-404	Sampler Vol [ml]:	10	Minute Vol [ml]:	552							
Nebulizer Flow [lpm]:	7.5	System Location:	119	Save Period:	0:05	Guyton Used:	No							
Sampler:	AGI-30	Hoodline ID:	4	Animal Number:	59-25	Required Dose:	2.57E+04	cfu						
Sampler Flow [lpm]:	6	Generator Number:	G	Weight [g]:	7500									
Exposure:	Time Calculated													
Animal Species:	NHP													
Agent:	Bacterial													
Time [sec]	RH [%]	Temp [C]	Press [WC"]	Conc [ug/L]	Hum Q [lpm]	2nd Q [lpm]	Neb 1 Q [lpm]	Neb 2 Q [lpm]	Pri Exh Q [lpm]	Sampler Q [lpm]	Sampler Q [lpm]	Tot In Q [lpm]	Tot Exh Q [lpm]	
5.268	21.299	26.648	0.153	0.069	0.104	8.434	7.786	0.17	10.17	3.808	3.808	16.493	13.978	
10.265	22.62	26.648	0.017	0.069	0.104	8.5	7.467	0.148	10.039	5.687	5.687	16.219	15.725	
15.272	25.952	26.685	-0.005	0.069	0.071	8.478	7.445	0.137	10.028	5.774	5.774	16.131	15.802	
20.27	30.09	26.685	0.033	0.215	0.093	8.511	7.456	0.148	10.039	5.84	5.84	16.208	15.879	
25.267	33.279	26.685	0.057	0.069	0.104	8.511	7.5	0.148	10.006	5.862	5.862	16.263	15.868	
30.264	37.893	26.685	0.024	0.069	0.082	8.489	7.5	0.137	10.028	5.884	5.884	16.208	15.912	
35.271	40.679	26.721	-0.003	0.069	0.093	8.533	7.5	0.148	10.039	5.895	5.895	16.274	15.934	
40.268	43.718	26.685	-0.047	0.655	0.082	8.511	7.489	0.126	10.05	5.906	5.906	16.208	15.956	
45.265	45.513	26.721	0.05	6.368	0.104	8.5	7.522	0.137	10.039	5.917	5.917	16.263	15.956	
50.263	47.71	26.721	-0.019	25.42	0.093	8.5	7.511	0.159	10.017	5.917	5.917	16.263	15.934	
55.27	49.541	26.721	-0.006	60.146	0.104	8.5	7.511	0.137	10.006	5.928	5.928	16.252	15.934	
60.267	50.679	26.721	-0.025	98.975	0.104	8.511	7.511	0.137	10.017	5.917	5.917	16.263	15.934	

580.265	57.783	26.978	0.026	188.203	0.082	8.511	7.511	0.159	10.028	5.972	5.972	16.263	16	
585.272	58.223	26.978	-0.012	188.35	0.082	8.5	7.522	0.159	10.039	5.983	5.983	16.263	16.022	
590.269	58.333	26.941	-0.002	189.229	0.093	8.544	7.522	0.159	10.028	5.972	5.972	16.318	16	
595.266	58.333	26.978	0.026	191.426	0.082	8.489	7.533	0.159	10.006	5.983	5.983	16.263	15.989	
600.264	58.369	26.978	0.05	192.012	0.104	8.511	7.533	0.159	10.006	5.972	5.972	16.307	15.978	
603.268	58.149	26.978	0.027	190.84	0.082	8.5	7.522	0.148	10.028	5.972	5.972	16.252	16	
E-Signature: Justin M. Hartings														
Original Data														
Wednesday, October 29, 2003														
11:56:54 AM Eastern Standard Time														



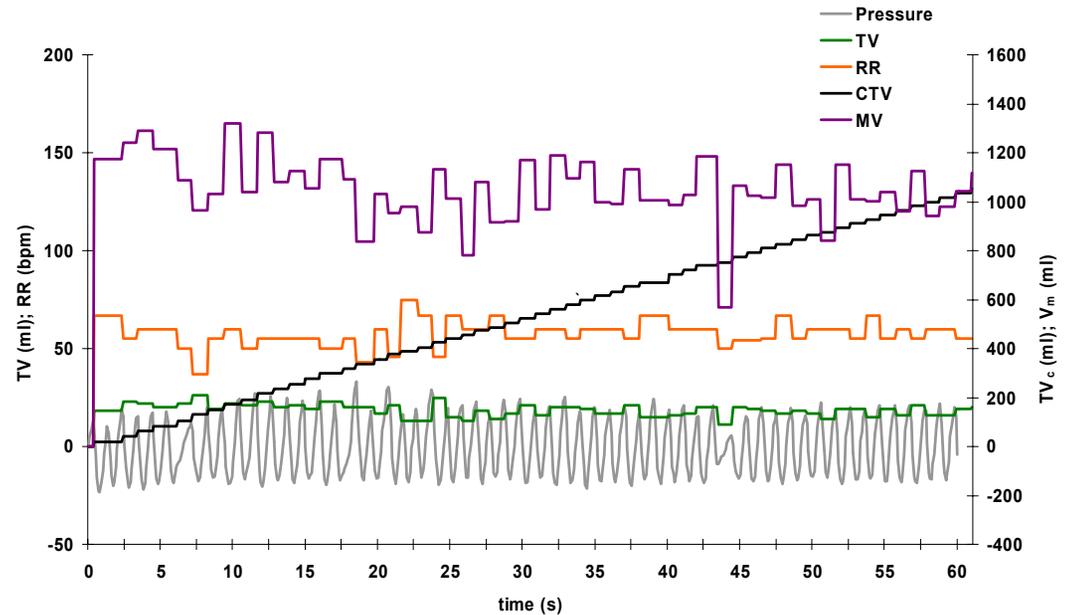
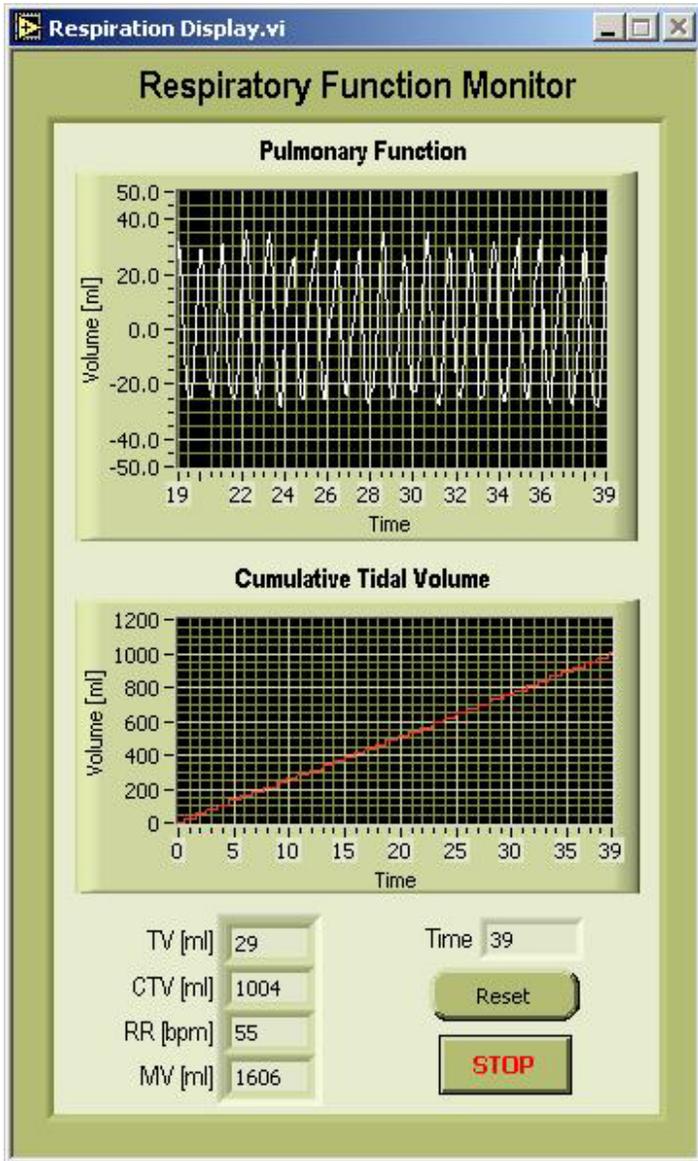
Respiratory Monitoring Module

- Controlled input and exhaust creates a sealed dynamic chamber
- For head-only exposures, animal respiratory tract functions as part of the chamber
- Animal respiration changes chamber volume
- Volume change produces pressure change detected by system hardware
- Pressure signal serves dual purpose
 - DC component used for system balancing
 - AC component used for respiratory monitoring



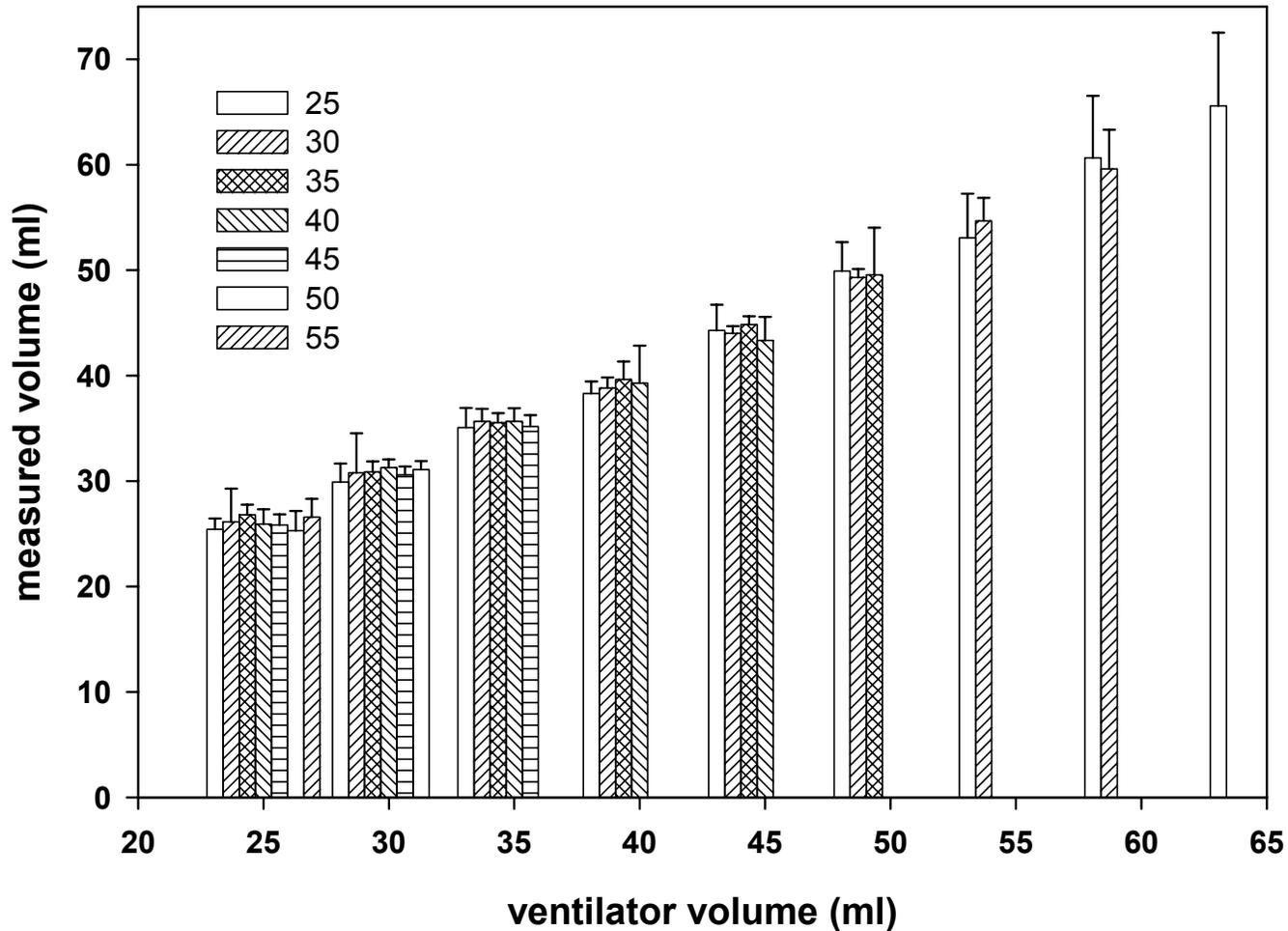


Respiration

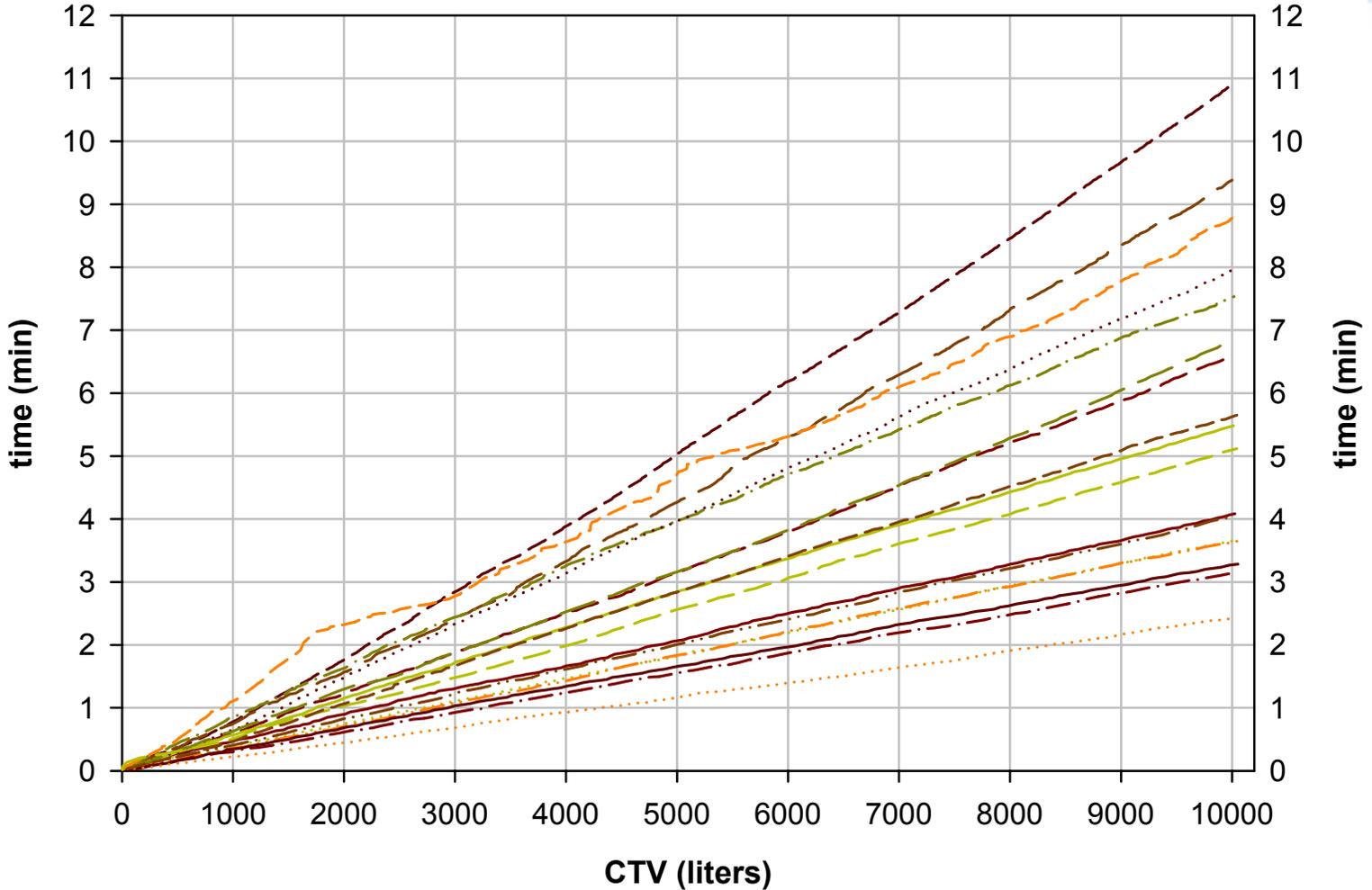




Respiratory Module Calibration



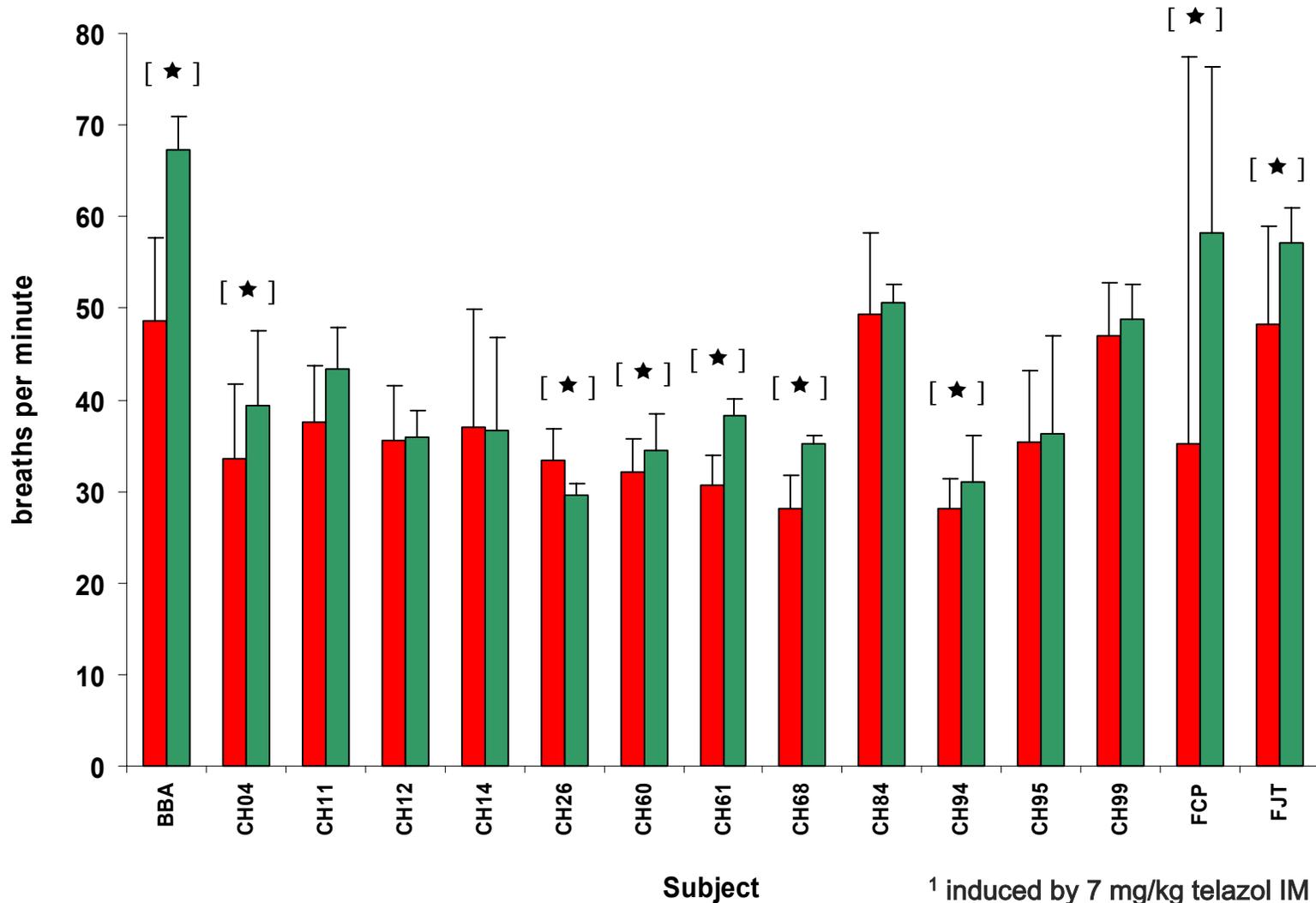
From Hartings and Roy, *In Press*



Cumulative tidal volumes (CTV) of sham-exposed anesthetized Rhesus macaques (n=15) utilizing the dosimetry function of the ABES. An arbitrary limit of 10,000 ml was preset to demonstrate breathing rate and depth differential in the primates under study.

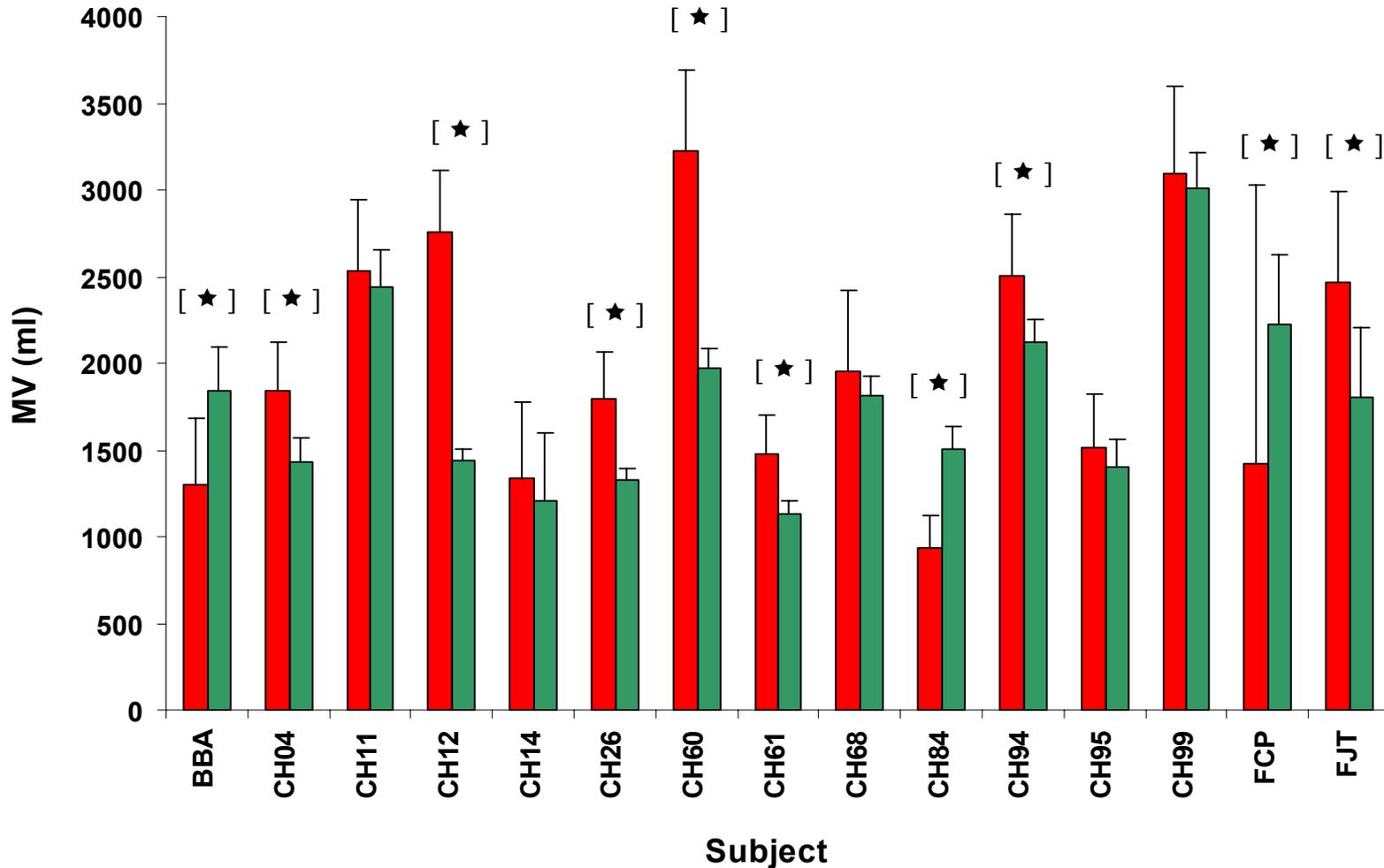


Mean *breaths per minute* of anesthetized¹ Rhesus macaques (n=15) using either whole-body plethysmography (red) or the ABES (green). Error bars represent standard deviation; significance at $p < 0.01$ denoted by asterisk and bracket (9/15).





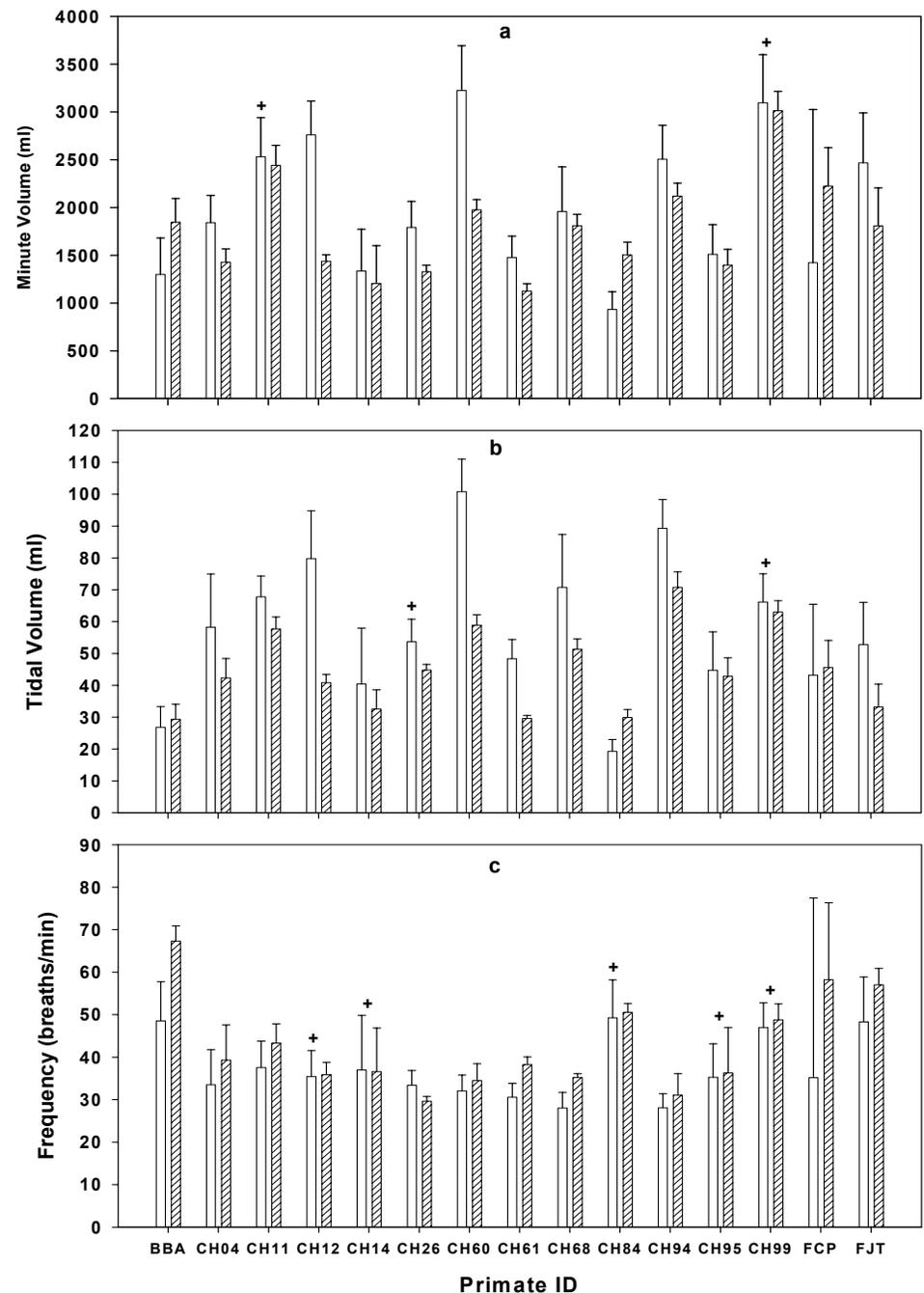
Mean *minute volume* of anesthetized¹ Rhesus macaques (n=15) using either whole-body plethysmography (red) or the ABES (green). Error bars represent standard deviation; significance at $p < 0.01$ denoted by asterisk and bracket (10/15).



¹ induced by 7 mg/kg telazol IM as needed



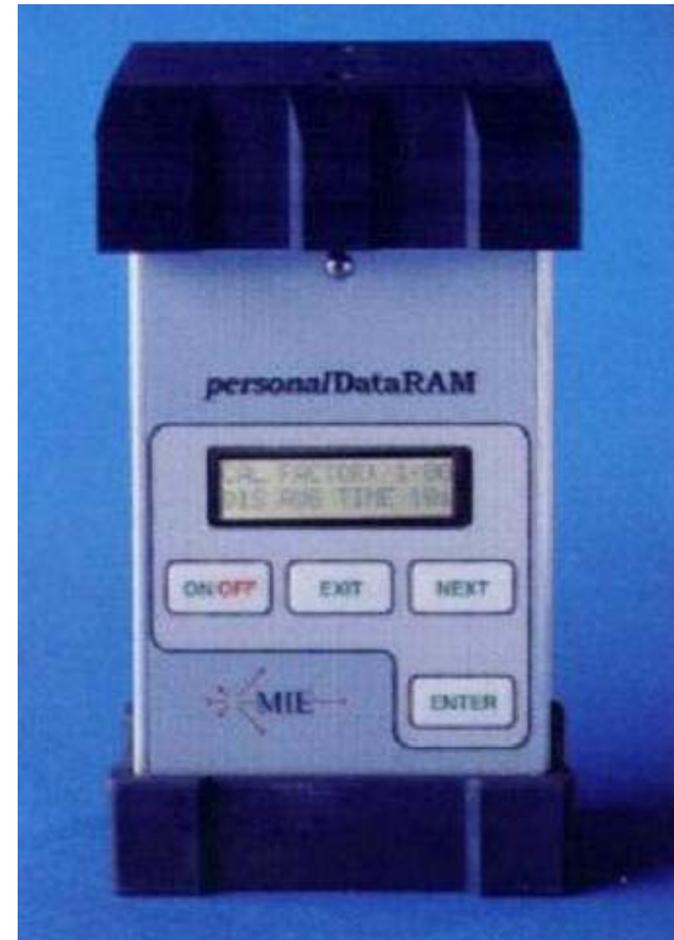
Comparison of minute volume (a), tidal volume (b), and respiratory frequency (c) measurements as determined by ABES and WBP in sham-exposed NHPs. Error bars represent standard deviation. Analysis using the Wilcoxon rank-sum showing no difference between methods is denoted by + at $p < 0.05$.





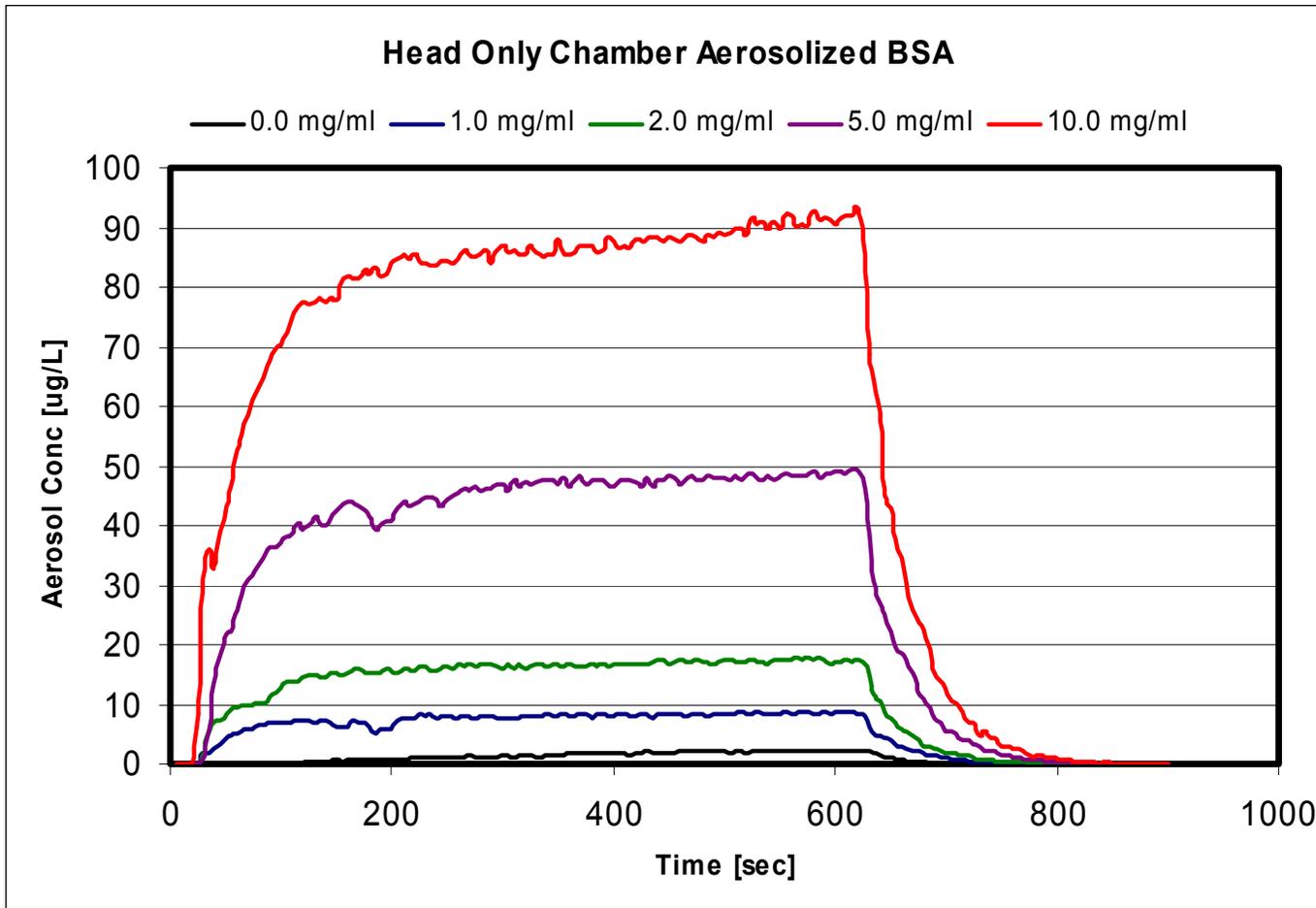
Aerosol Concentration

- Passive air sampling
- Real-time monitoring
- Optical scattering
- Commonly used in personal monitoring
- 0.001 to 400 mg/m³ autoranging
- Digital or analog output
- Ideal for Automated System





Concentration Monitoring





Real-Time Dosing for Toxins

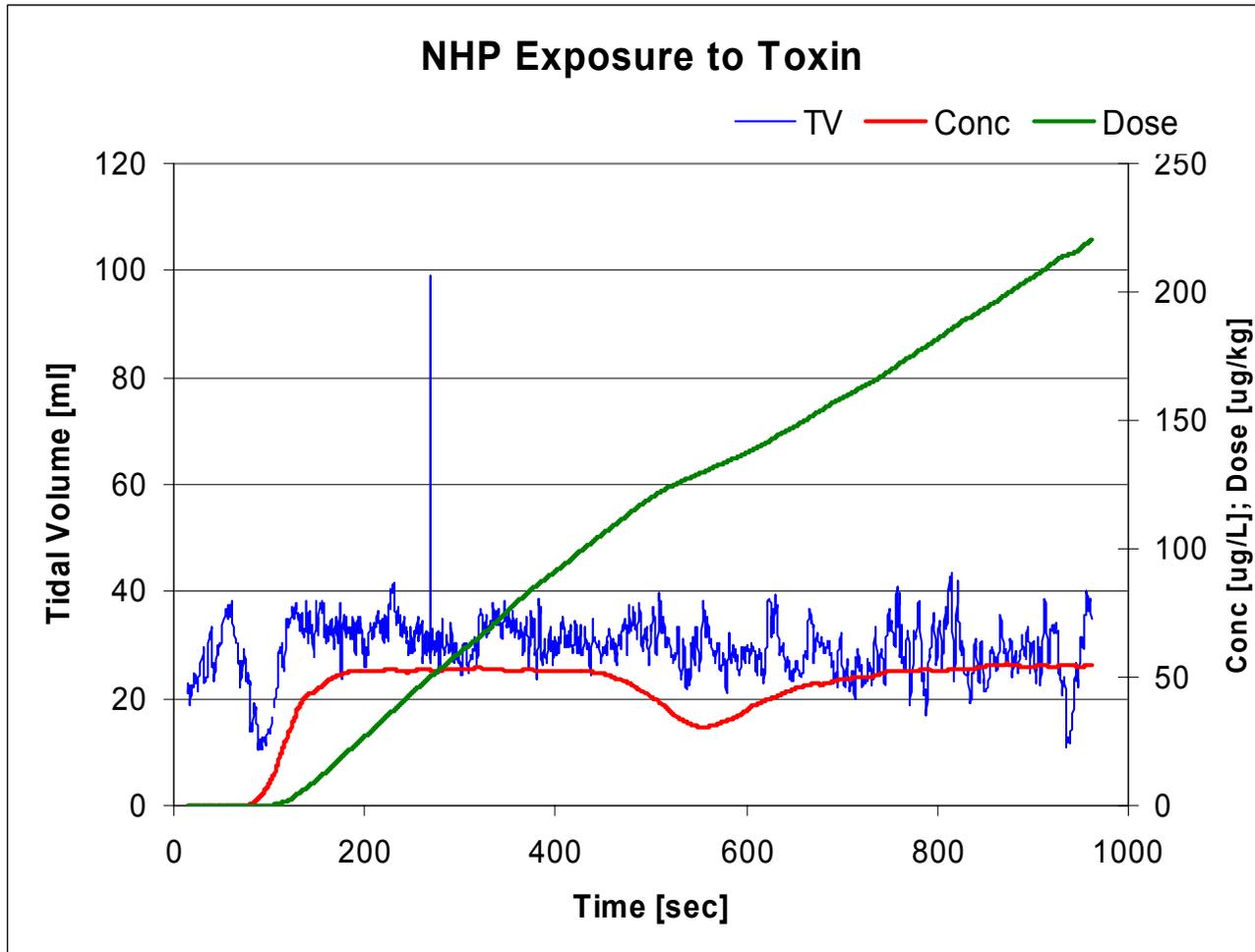
- Combine DataRAM results with respiratory measurement
- Calculate discrete dose in real-time for each breath

$$D = \sum_{n=1}^m R_n \times C_n$$

- Automatically terminate exposure when requisite dose is achieved
- NHP exposure to toxin
 - Target dose of 220 $\mu\text{g}/\text{kg}$
 - Collect with AGI to compare dose results



Real-Time Dose Control



AGI Results: $D = 210 \pm 20 \mu\text{g/kg}$